

Inventors: Hansen et al.  
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AMENDMENTS

In the specification:

On page 4, please delete the paragraph on lines 21-22 and substitute therefor:

Figure 4 shows a multiple alignment of *E. Coli* DXPR (SEQ ID NO:1) to *S. aureas* homoserine dehydrogenase (1EBF\_A) (SEQ ID NO:2).

On page 78, please delete the paragraph on page 78, line 15, to page 79, line 12, and substitute therefor:

Sequence comparison signatures were determined for the NAD(P)-binding sequences (including 28 DXPR sequences) in the Swiss-Prot database [[12]] and clustering was performed as described in Examples I and II. The 28 DXPR sequences formed one cluster. When visualized in a comparison matrix, the DXPR cluster was proximal to other clusters. These other clusters were composed of aspartate semialdehyde dehydrogenase, homoserine dehydrogenase, N-acetyl-g-glutamyl phosphate reductoisomerase, or glyceraldehyde 3-phosphate dehydrogenase; all of which share a common NAD(P)-binding Rossmann fold. The proximity correlated with local sequence identity between DXPR sequences and sequences of these other clusters, ranging

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from about 17 to 40% local sequence identity. Although the E-scores of these sequence identities were between 0.1 and 2.0, these clusters were identified as related groups because multiple DXPR sequences systematically showed cross-talk to only the above mentioned sequence clusters. In particular, cross-talk was identified as low sequence identity (less than 30%) between the cluster containing DXPR and a few sequences belonging to other clusters, which showed a pattern that was distinct from a pattern observed in the cluster. The cross talk was distinguishable from true noise because in the case of noise, only a single DXPR sequence had low similarity to some other cluster. Based on these data, the NADP-binding domain of *E. coli* DXPR was predicted to contain a Rossmann fold.

On page 79, please delete the paragraph on page 79, line 26, to page 80, line 11, and substitute therefor:

A multiple-alignment of *E. coli* DXPR with the NAD-binding domain of *S. cerevisiae* homoserine dehydrogenase was performed using Clustalw (Thompson et al., Nucl. Acids. Res. 22:4673-4680 (1994)). The NAD-binding motif of *E. coli* DXPR (LGXTGSIG; SEQ ID NO:3) aligned very well with the NAD-binding motif of *S. cerevisiae* homoserine dehydrogenase (IGAGVVGS; SEQ ID NO:4) as shown in Figure 4. This alignment was used to build several models of *E. coli* DXPR using the MODELER module in

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MSI Insight II (Sali and Blundell, J. Mol. Biol. 234:779-815 (1993)). The model having the least coiling of loops was chosen and is shown in Figure 5, with some NADP-contact residues colored in blue (isoleucine), black (methionine), and cyan (lysine). The bound conformation of NAD from homoserine dehydrogenase is superimposed on the model and shown in green.